



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

[DATE \@ "MMMM d, yyyy"]

DRAFT DELIBERATIVE; INTERNAL ONLY

By Certified Mail

Return Receipt Requested

Keith A. Matthews, Agent
C/O Oxitec, Ltd
Wiley Rein LLP
1776 K St. NW
Washington, DC 20006

Subject: 90-day Preliminary Technical Screening Results
OPP Decision Number: 537030
EPA File Symbol: 93167-EUP-R
Product Name: OX513A *Aedes aegypti*
Application Receipt Date: December 4, 2017
EPA Company Number: 93167
Company Name: Oxitec, Ltd

Dear Mr. Matthews:

The U.S. Environmental Protection Agency (Agency or EPA) has completed its preliminary technical screening of your application pursuant to Section 33(f)(4)(B)(i)(II) of the Federal Insecticide, Fungicide, and Rodenticide (FIFRA) Act, as amended by the Pesticide Registration Improvement Extension Act. The Agency has determined that your application has not passed the preliminary technical screen and therefore is subject to rejection if the application is not corrected.

The attached confidential appendix describes the data and/or information Oxitec, Ltd will need to provide to the EPA to correct the application. EPA provides below some additional details on the results of the preliminary technical screen.

- A search of the AllergenOnline database (Version 18A, February 01, 2018) found DsRed2 to have significant homology to a putative allergen (GFP-like protein; Kato *et al.*, 2017). Thus, allergenicity of the modified DsRed2 cannot be excluded and human exposure to the protein must be addressed.

- Preliminary analysis of the presented penetrance data, combined with the proposed maximum release rate of OX513A mosquitoes, indicates the potential for humans to be exposed to adult OX513A female mosquitoes.
- The presence of tTAV and DsRed2 proteins in mosquito saliva and subsequent human exposure cannot be ruled out due to uncertainties in assay methodologies. Use of *E. coli* produced DsRed2 and tTAV proteins as positive controls are not sufficient to ensure the validity of the assays, particularly in light of a lack of detection of mosquito/endogenously produced DsRed2 and tTAV proteins in whole mosquito larvae and adult assays.
- Validation controls for the whole mosquito larvae and adult assays were poor and the assays display unexplained discrepancies. For example, DsRed2 can be detected in OX513A larvae by making use of its ability to fluoresce at certain wavelengths. These DsRed2 containing red larvae can be seen under a microscope with the human eye. However, the assay data supplied by Oxitec shows that the DsRed2 protein in fluorescing red larvae cannot be detected, rendering the whole mosquito larvae and adult protein assays questionable.
- A CBI redacted version of FDA's Assessment was submitted to the EPA by Oxitec suggesting at least some data supporting the FDA assessment were not submitted to EPA including data/information which may fulfill some of the deficiencies listed for this application.

For the review of your product to continue, you will need to correct your application to address the items listed above within 10 business days of the date you received this letter. Corrections must be received by EPA by the 10th business day. EPA recommends sending your complete set of corrections by email to the contact listed below to ensure they are timely received. If studies or confidential information are being submitted by mail, a complete courtesy copy, minus confidential information, received by email by the deadline will be considered timely. If you cannot correct the application [or do not respond] within 10 business days, your application will be rejected. At this time, you could also choose to withdraw your application.

If you have questions, please contact Eric Bohnenblust at [[HYPERLINK "mailto:Bohnenblust.eric@epa.gov"](mailto:Bohnenblust.eric@epa.gov)] or (703) 347-0426.

Sincerely,

Alan Reynolds, PM 94
Emerging Technologies Branch
Biopesticides and Pollution
Prevention Division (7511P)